1004-125 Fluid Viscosity Affects the Persistence and Size of Echocardiographic Contrast Agents: Insights into the Mechanism of Resonance-Induced Microbubble Destruction

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Acoustic microbubble destruction is thought to be a consequence of microbubble resonance behavior, although the mechanism of this phenomenon remains unclear. Since fluid viscosity (FV) is an important theoretical determinant of parameters which affect microbubble resonance behavior (e.g. oscillation amplitude and frequency), we hypothesized that microbubble *persistence* is affected by FV. *Methods:* Microbubble persistence was determined using an optical particle sizing system capable of precisely quantifying microbubble number and size during and following exposure to ultrasound. The in vitro apparatus consisted of a well-mixed reservoir containing 100 ml of a blood analog fluid (aqueous glycerin solution) to which 0.05 ml of Albunex® or FS069 (Molecular Biosystems, San Diego, CA) was injected. At variable FV (1–3 cP), the chamber was insonated continuously at various transmit powers (20–100% of max.). Microbubble counts were recorded every five seconds until the number of microbubbles decayed by 90%. Particle count versus time data were fit to an exponential decay function and particle half-life ($T_{1/2}$) calculated for each condition. Additionally, microbubble size distributions were generated following transient exposure (5 seconds) for each condition and compared. *Results:* For a constant transmit power, particle $T_{1/2}$ increased with increasing FV ($p < 0.0001$). At a FV of 3cP, FS069 $T_{1/2}$ increased four fold compared to the 1cP sample. Additionally, even at low to moderate transmit powers, mean microbubble diameter decreased following transient exposure ($p < 0.01$), with this effect being more marked at lower FV. FS069 persisted longer than Albunex® for each condition ($p < 0.01$). *Conclusions:* Microbubble persistence and size are affected by fluid viscosity during transient and continuous exposure to ultrasound. These results may be important in patients with abnormal blood viscosities and provide additional insight into mechanisms of acoustic microbubble destruction.

1004-126 Cold Temperature Augments Albumin Microbubble Adherence to Cardioplegia-Perfused Human Coronary Endothelial Cells

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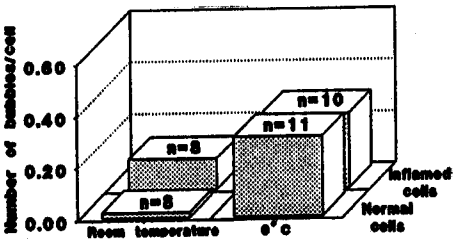
During cold cardioplegia (CP) delivery, albumin microbubbles used in myocardial contrast echocardiography persist in the myocardium. Using a culture medium-perfused endothelial cell (EC) preparation, we have shown that EC inflammation increases bubble adhesion, and that CP further augments adherence when ECs are perfused at room temperature (temp). To test the hypothesis that *cold* CP temp independently affects microbubble-EC adherence, coverslips with cultured human coronary artery ECs were exposed to 0ºC crystalloid CP for 10 min, mounted in a parallel plate system, and perfused for 3 min with fluorescein-labeled Albunex suspended in CP. Control coverslips were subjected to 3 min CP perfusion only, without prior exposure to cold CP. Perfusions ware performed with or without prior EC inflammation with phorbol ester, and bubble adherence was quantified in 30 fields/coverslip using fluorescent videomicroscopy.



In normal ECs, cold CP significantly increased the extent of bubble adhesion ($p < 0.001$) (Figure). Although at room temp, EC inflammation was associated with increased bubble adherence compared to baseline ($p < 0.001$), exposure of inflamed EC to cold CP caused a further, insignificant increase in adhesion ($p = 0.25$). After EC exposure to cold CP, bubble adherence to normal vs inflamed ECs was comparable ($p = 0.92$).

Exposure of normal endothelial surfaces to CP at cold temp augments Albunex adherence to ECs beyond that seen at ambient temp, and the extent of adherence quantitatively parallels that seen in fully activated cells. These data suggest that cold temp *per se* may initiate an EC inflammatory-like response permissive towards bubble adhesion, and may contribute to in-vivo observations of delayed microbubble transit in cold-CP perfused hearts.

1004-127 Short Pulses of Ultrasound Can Reduce Echocontrast Reflectivity Up to 99%: Implications for Quantitative Contrast Echocardiography

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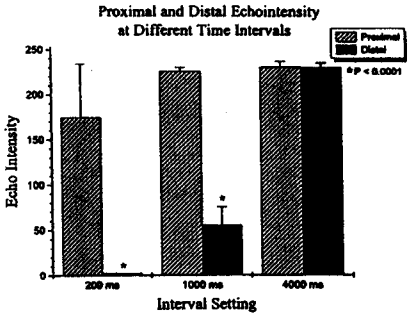
The utility of microbubbles as true flow tracers may be limited if they are acoustically labile, especially if reflectivity declines rapidly during imaging. We pumped a constant concentration of Aerosomes™ echocontrast agent at a velocity of 1.4 cm/sec through an in vitro model consisting of a thin walled rubber tube encased in agar. The tube was imaged along the long axis with a prototype Hewlett-Packard (HP) 1.8 MHz transducer and an HP SONOS 2500 echocardiography machine capable of harmonic and gated imaging which produced 35 msec gated pulses of ultrasound energy at variable pulse intervals. Gain (output) was set in a mid level; spatial peak pulse average of 25 W/cm^2. Gating was set at 200 msec intervals (which permitted only partial replenishment of the tube's fluid column between pulses) and *stepped* toward 4000 msec (which permitted complete replenishment), a clear boundary between the replenishment wave front moved stepwise across as gating interval was increased. On-line acoustic density analysis demonstrated a 99% decline in intensity across the model when pulsed every 200 msec ($p > 0.0001$, Fig.).



These findings demonstrate that acoustic pulses as short as 35 msec can virtually abolish reflectivity.

1004-128 Attenuation of Echo-Contrast Using Albunex is Linearly Related to Exposed Ultrasound Power

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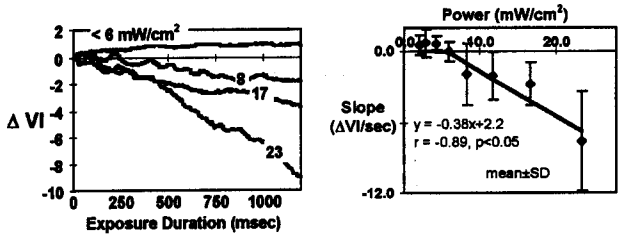
Continuous exposure to ultrasound reduces reflectivity of echo contrast agents, but the quantitative relationship between transmitted power and contrast destruction is unknown. *Methods:* An in vitro model was filled by a contrast suspension of 0.2% of Albunex (Mallinckrodt Medical) in 5% dextrose. A 7.5 MHz ultrasound transducer was applied to the surface of the suspension, and video output (168 frames/sec, Toshiba SSA-380) linearly digitized into 256 video intensity (VI) levels. Transmitted power was changed from 2.1 mW/cm^2 (Spatial Peak/Time Average) to 23 mW/cm^2 (8 levels, 10 runs each) and the data analyzed by multilinear regression of VI vs. time and power.



Results: VI decayed linearly with time, and decayed faster for higher power (left figure); the slope of VI decay was linearly related to power ($r = -0.89$, $p \leq 0.05$) above a threshold of 6 mW/cm^2 (right figure). *Conclusion:* 1) Below a threshold of mW/cm^2, Albunex is not significantly affected by exposure to ultrasound, but destruction rises linearly above this power. 2) Adjustment of transmitted ultrasound power may allow continuous imaging of echo contrast.

TUESDAY POSTER